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# Combinatorial compound library

- 15,000 compounds screened; collection growing
- Novel "drug like" molecules by Lipinski's "rule of 5"
- Based on 125 templates, 200 congeners each

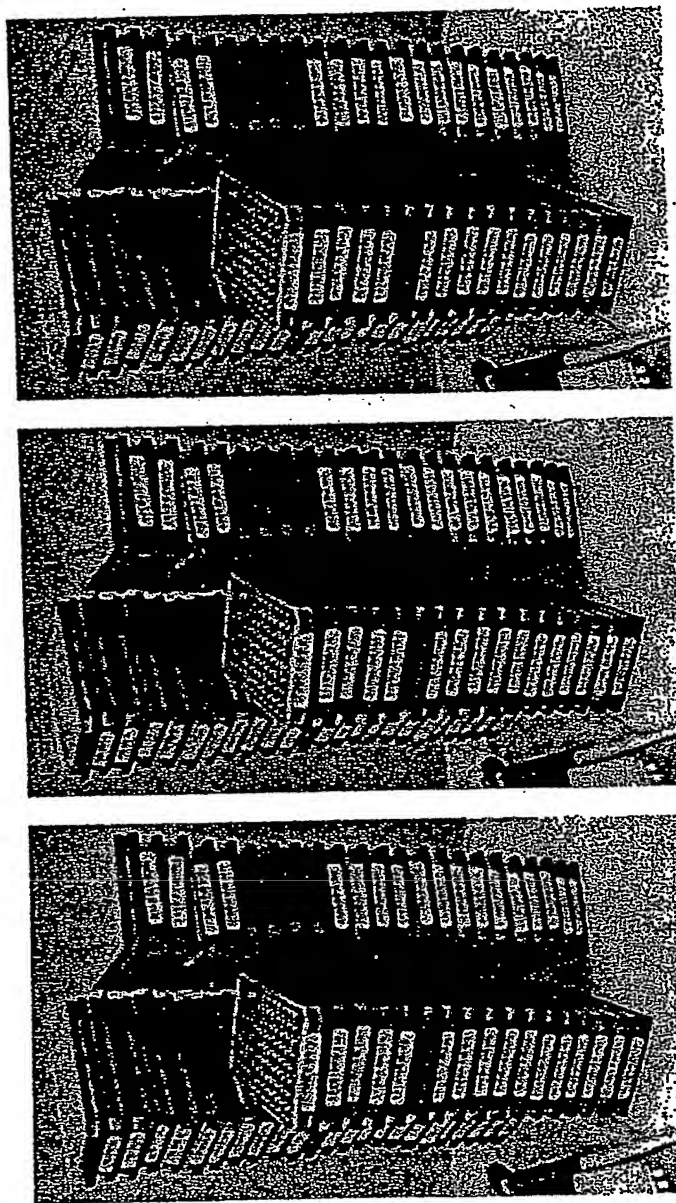
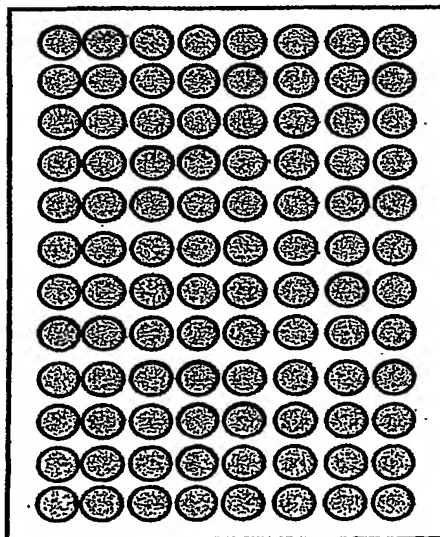


Figure 1

# Screening scheme

assay mix/compound/mix



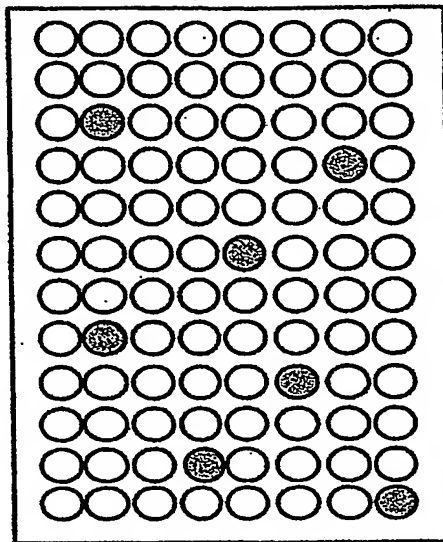
$1.5 \times 10^4$  neutrophils/well

incubate with test agents

37C for 30 min; add TNF

90 min at 37°C

(T90)

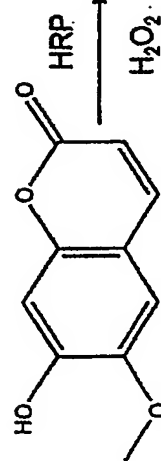


Inhibitors of TNF specific  
signaling molecules

Toxicity to neutrophils

Inhibitors of the assay itself (HRP)

Intrinsic fluorescence



6-methoxy 7-hydroxy coumarin

Non-fluorescent

HRP

$H_2O_2$

Figure 2

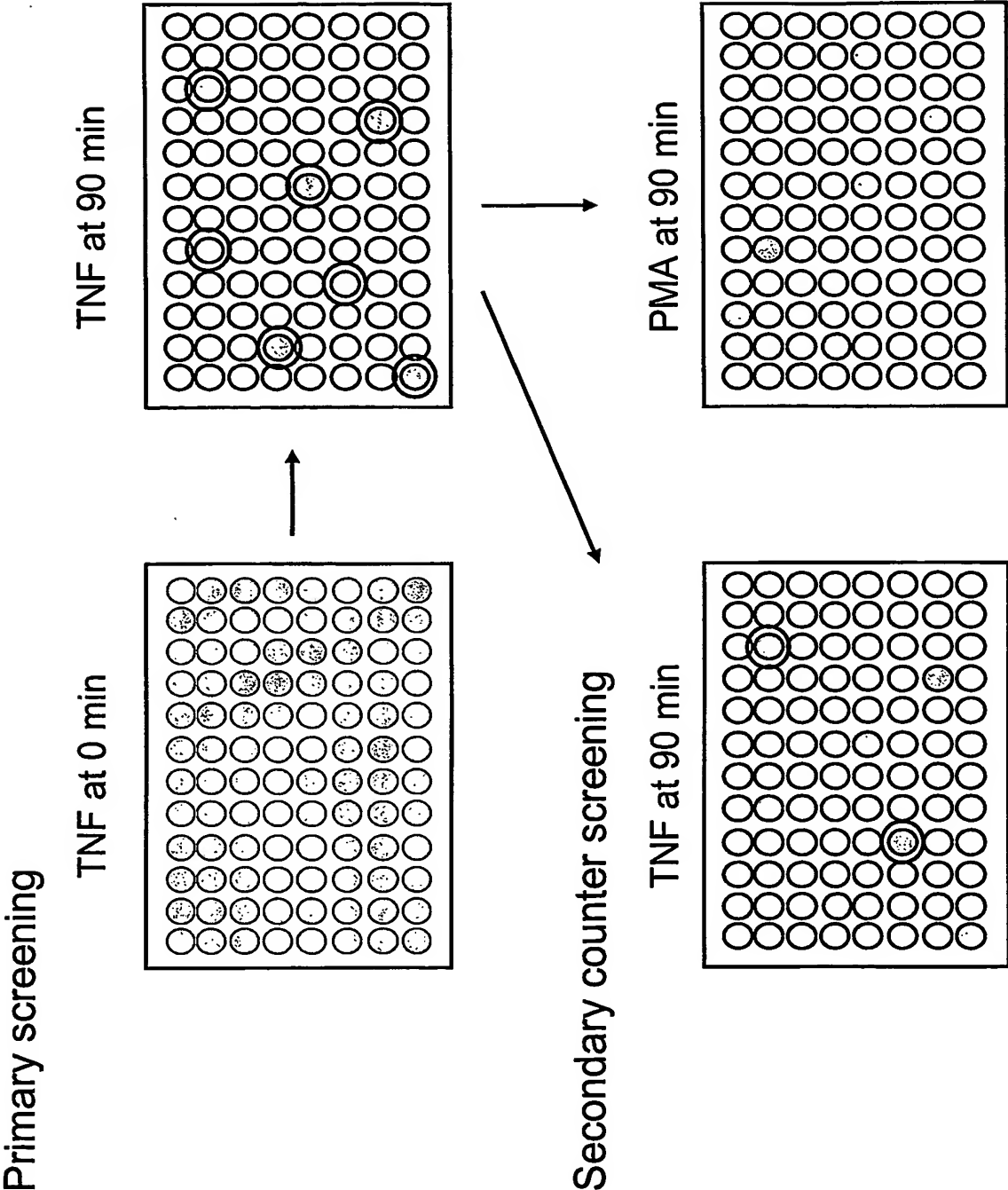


Figure 3

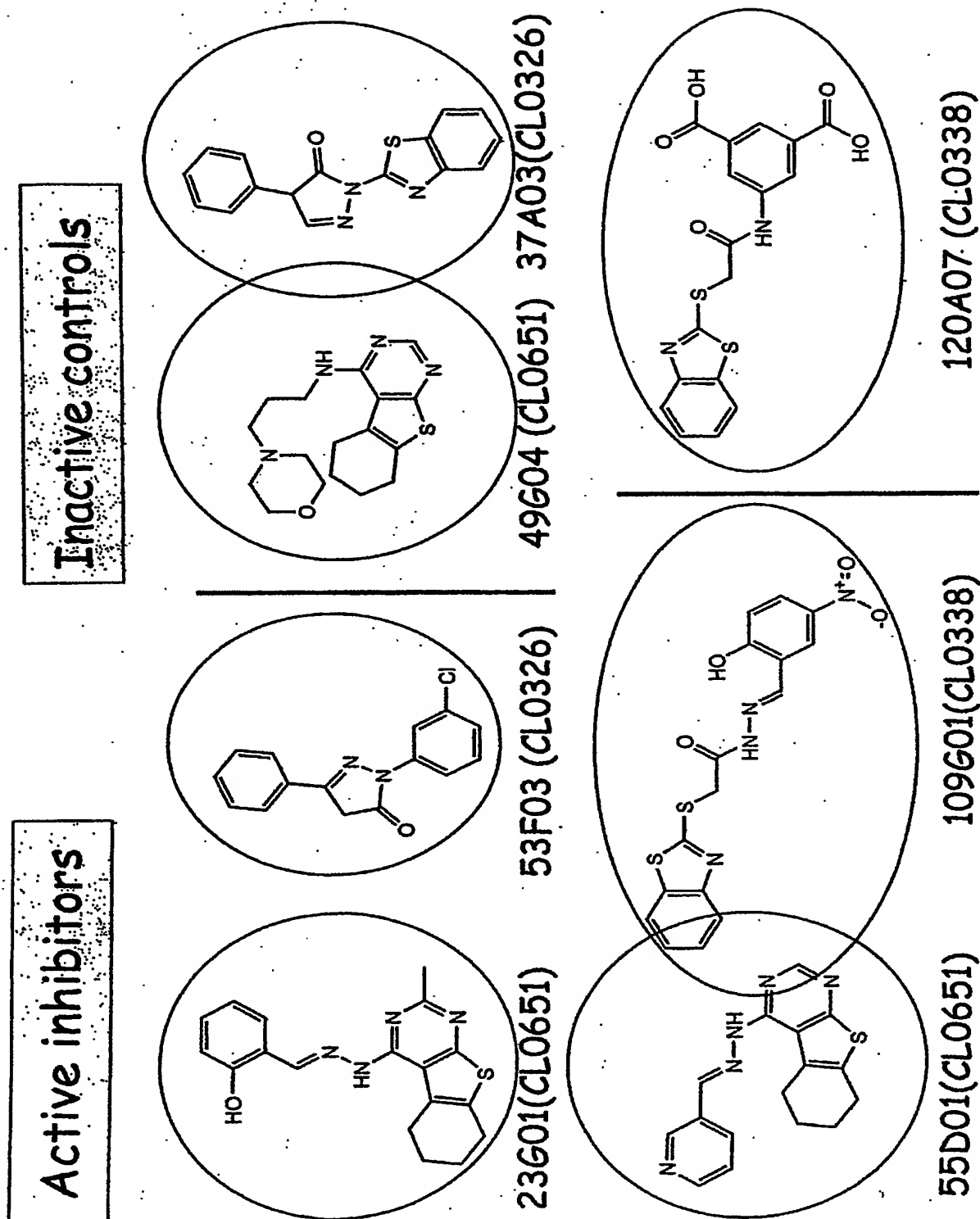


Figure 4

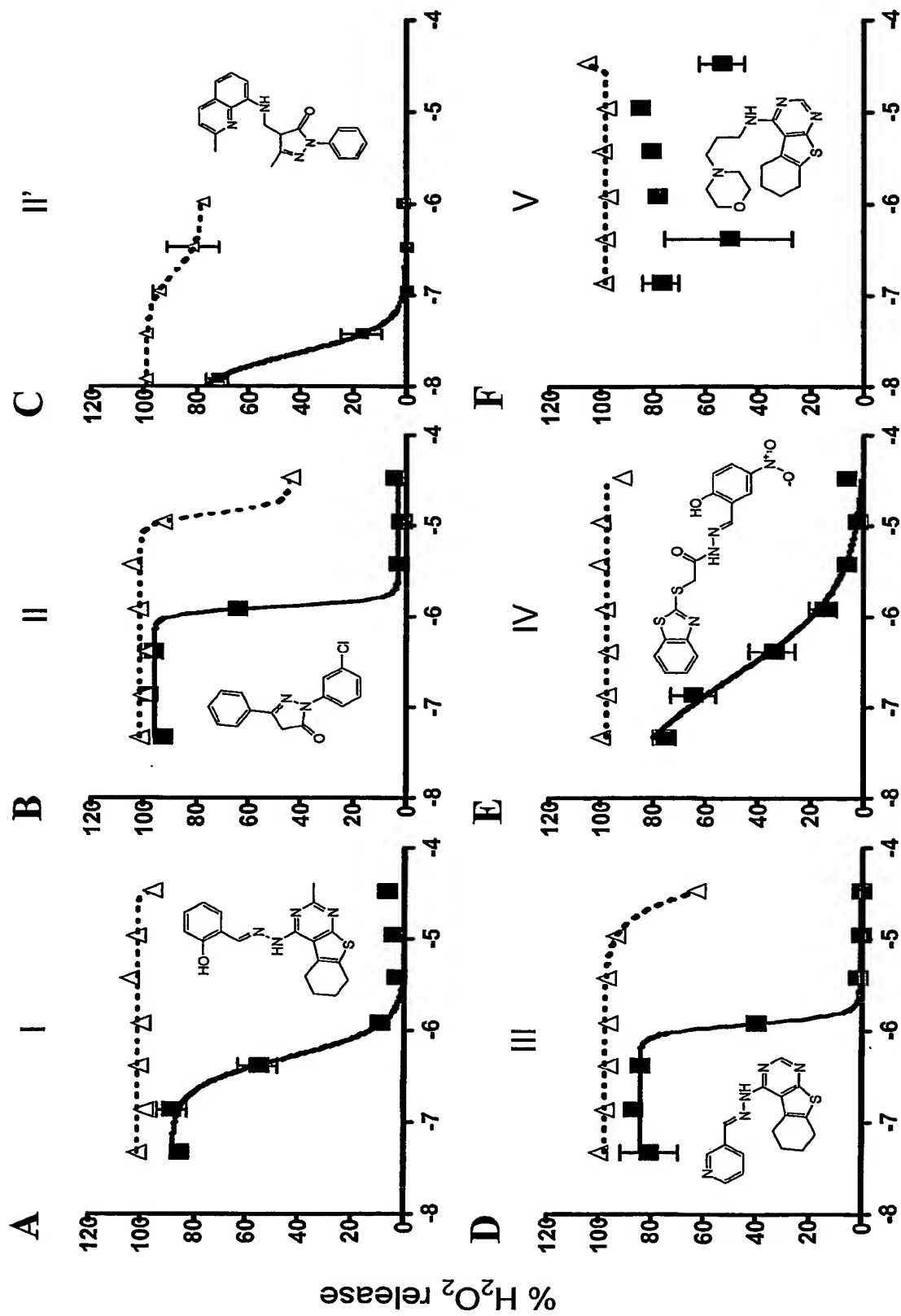
 $\log_{10}$  [compound] M

Figure 5

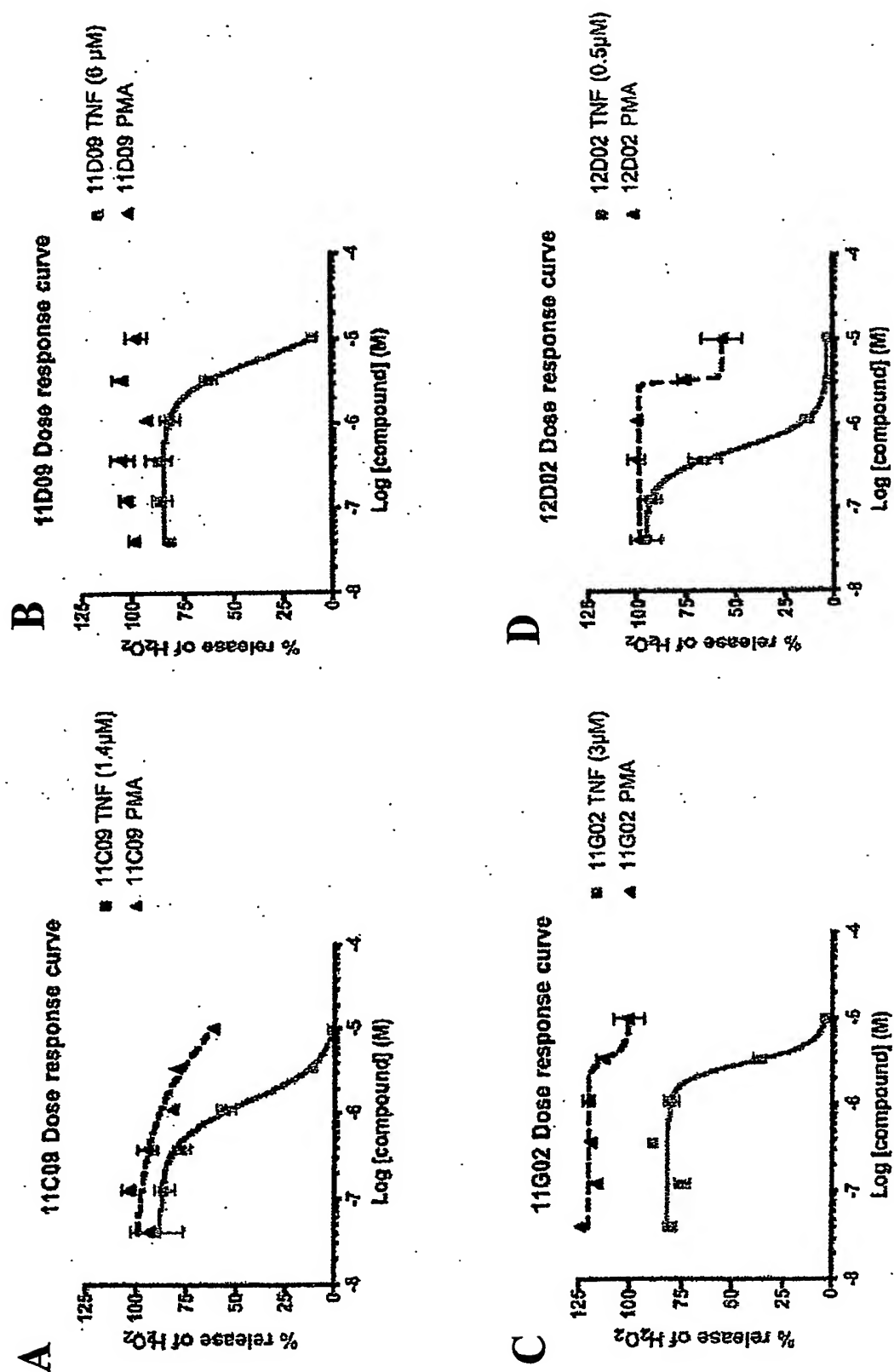


Figure 6

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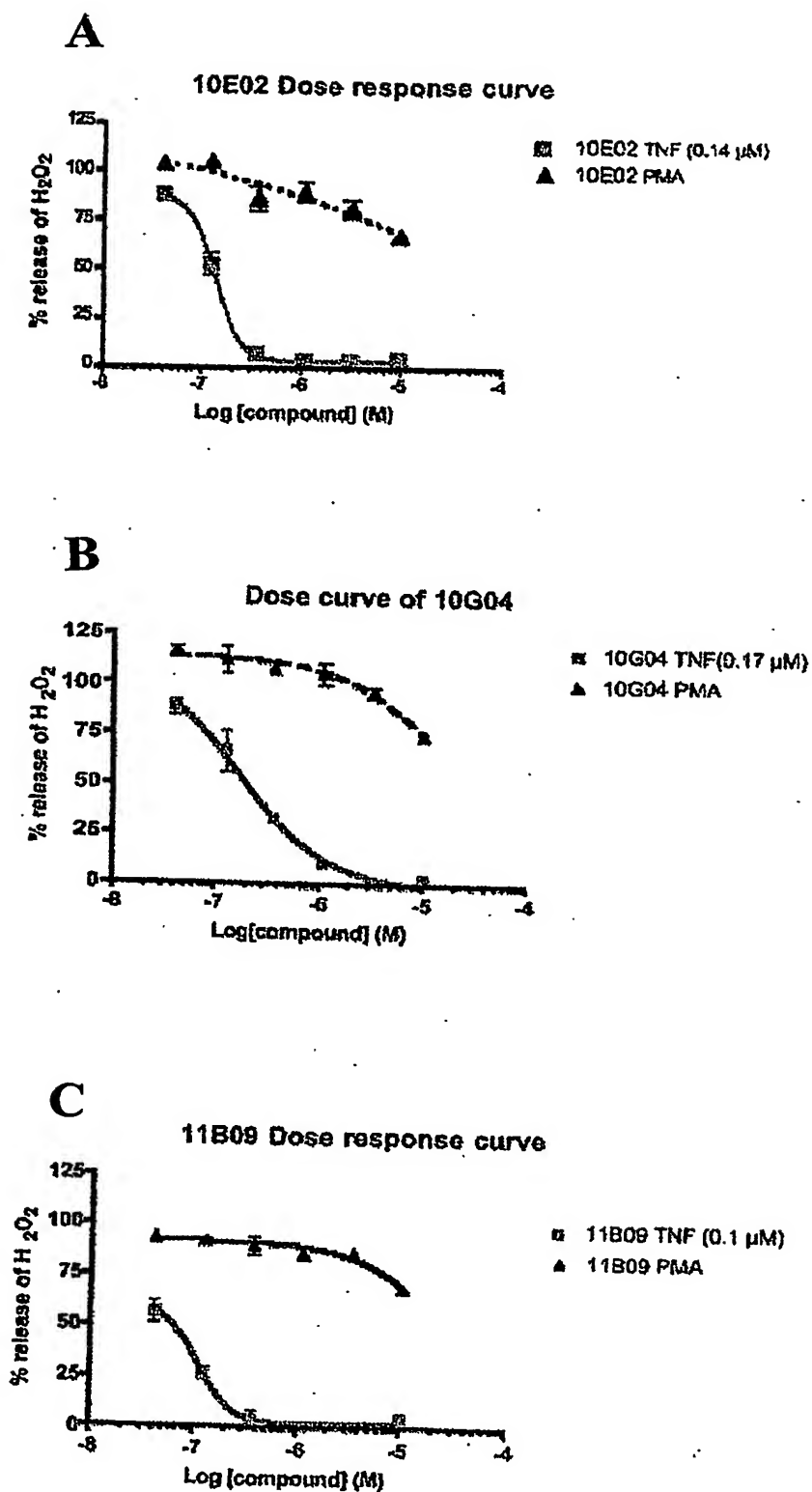


Figure 7

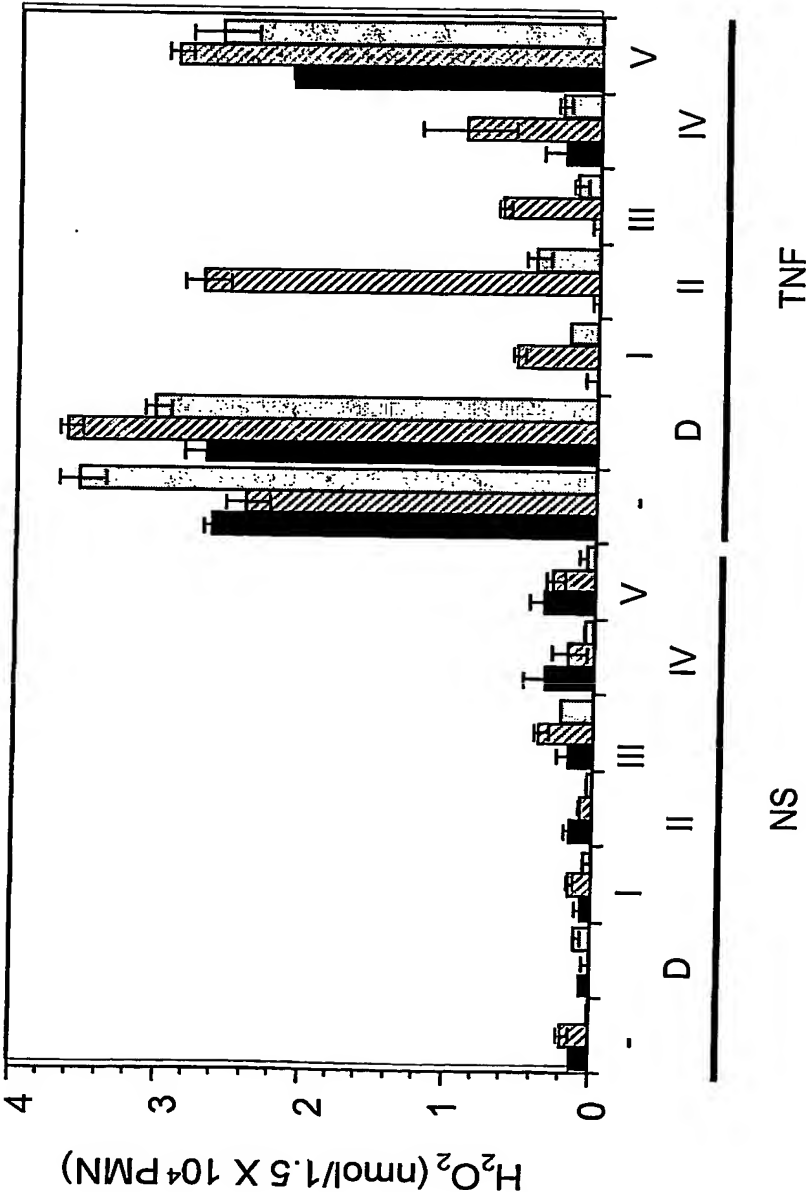
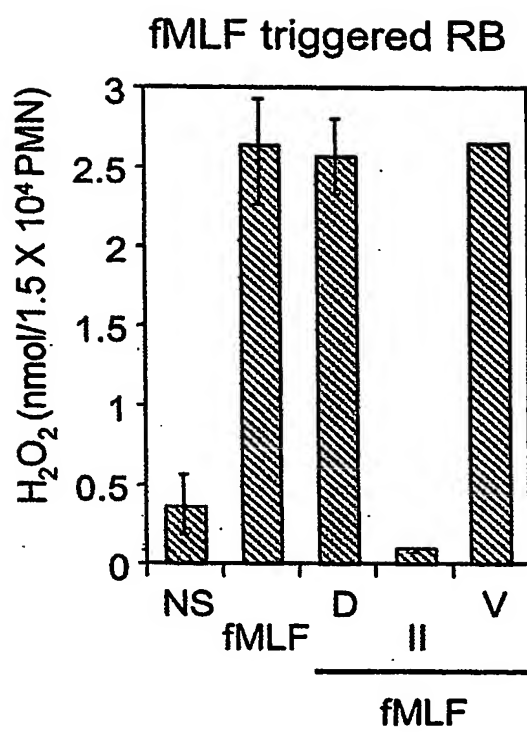


Figure 8



**Figure 9A**

fMLF Triggered RB

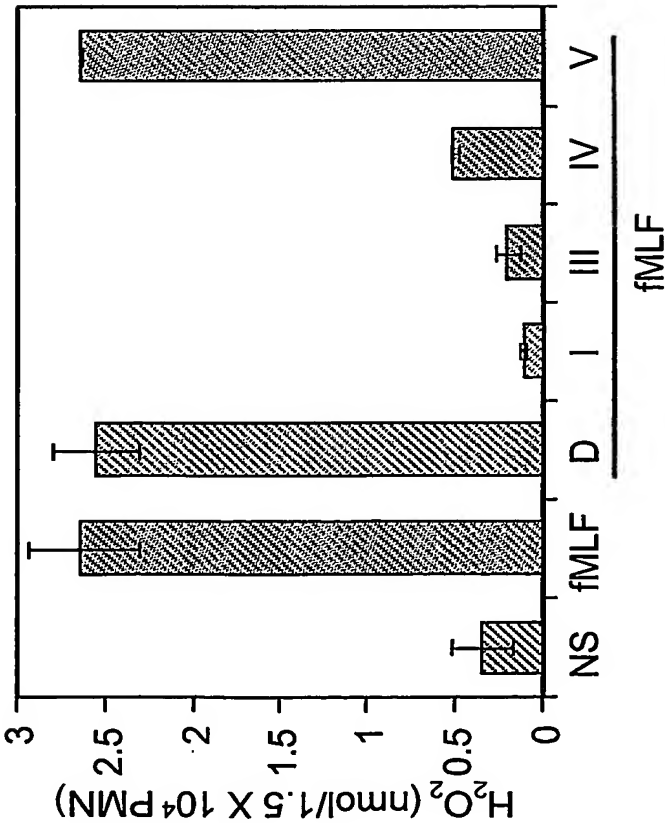


Figure 9 B

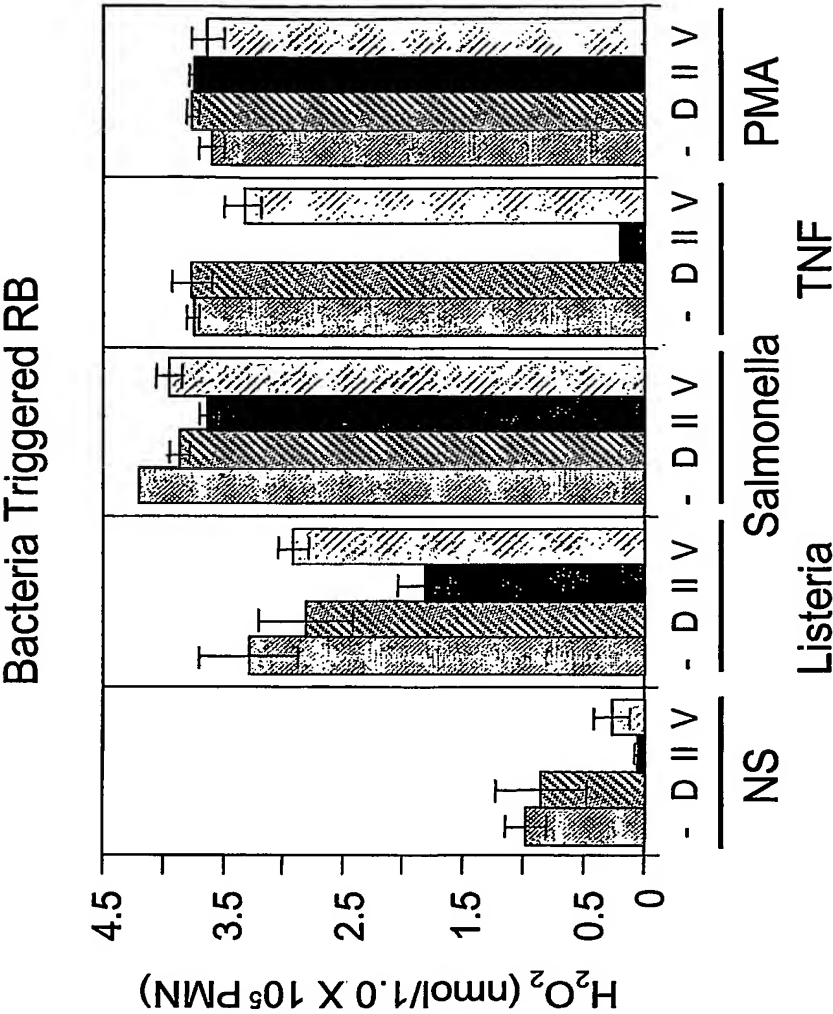


Figure 10A

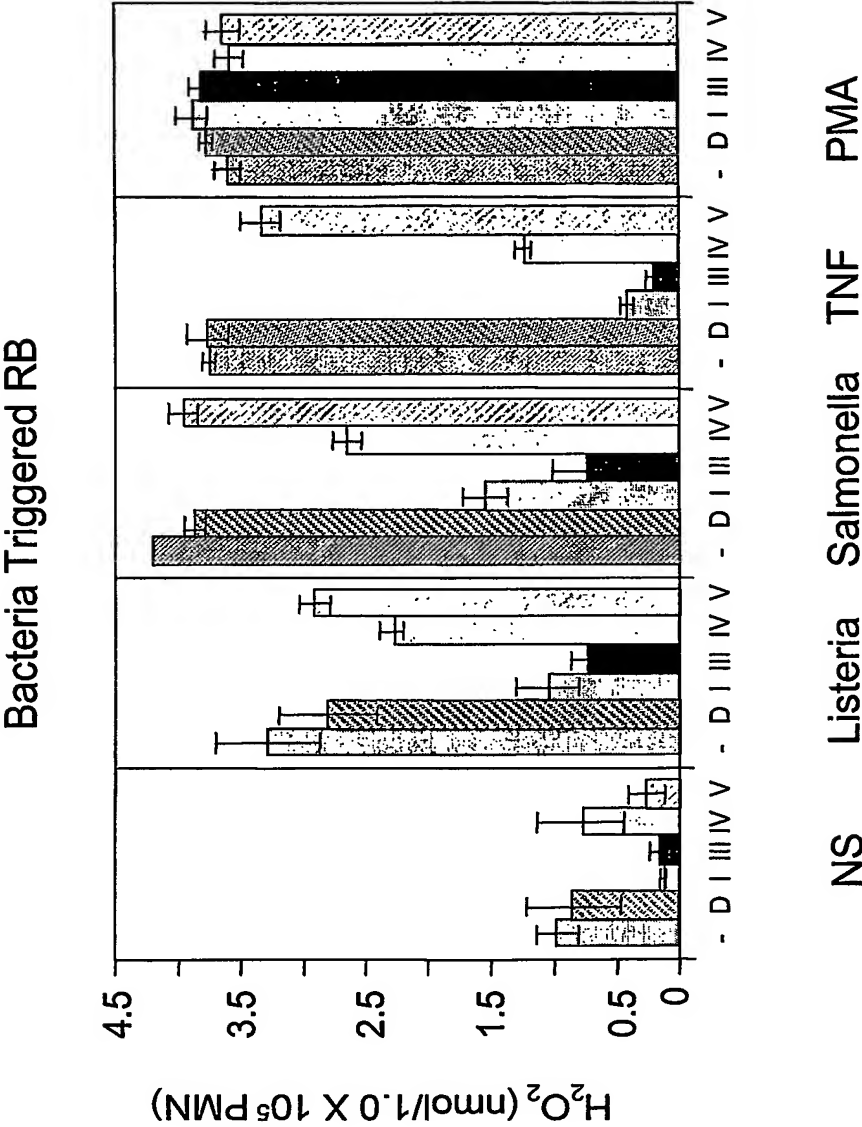
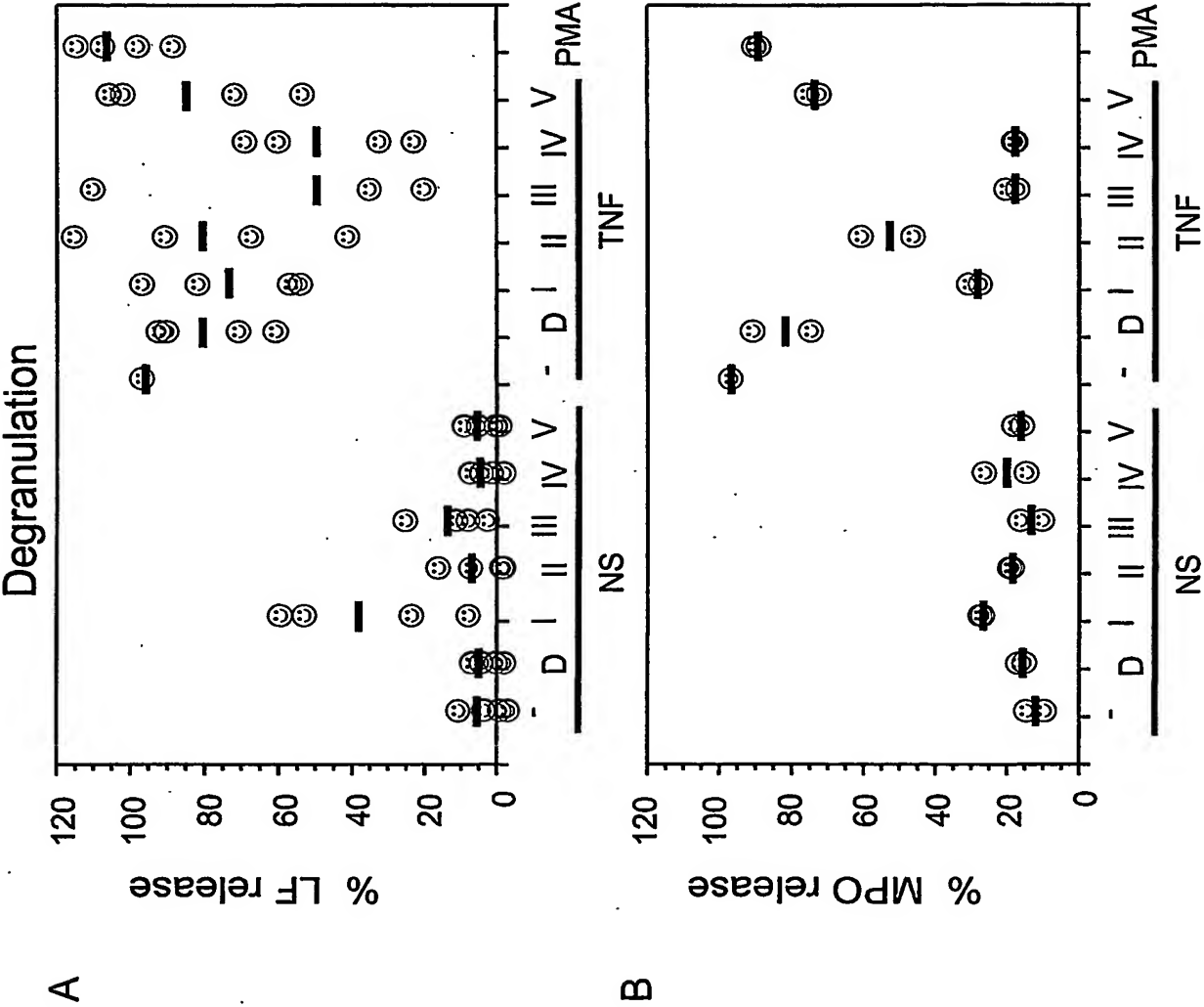


Figure 10B



**Figure 11**

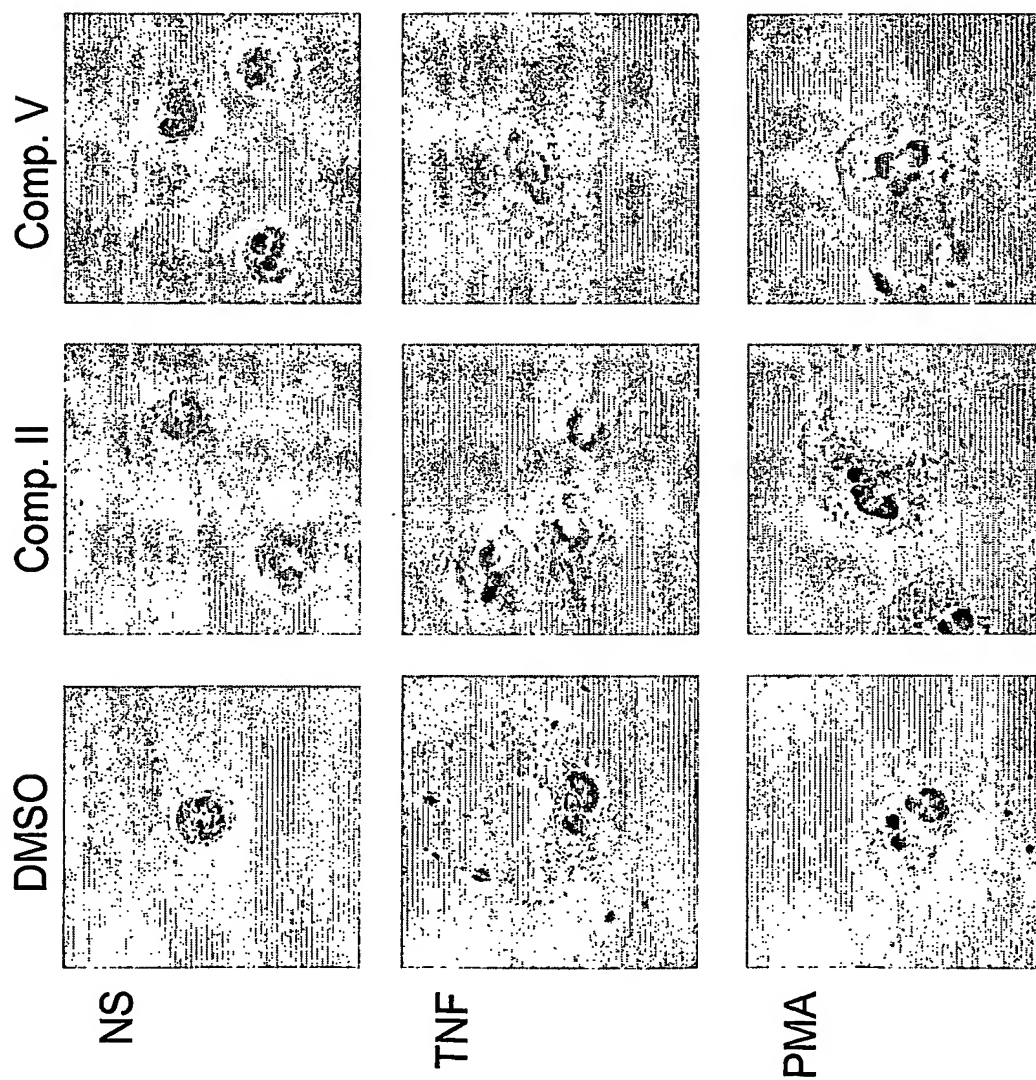


Figure 12A

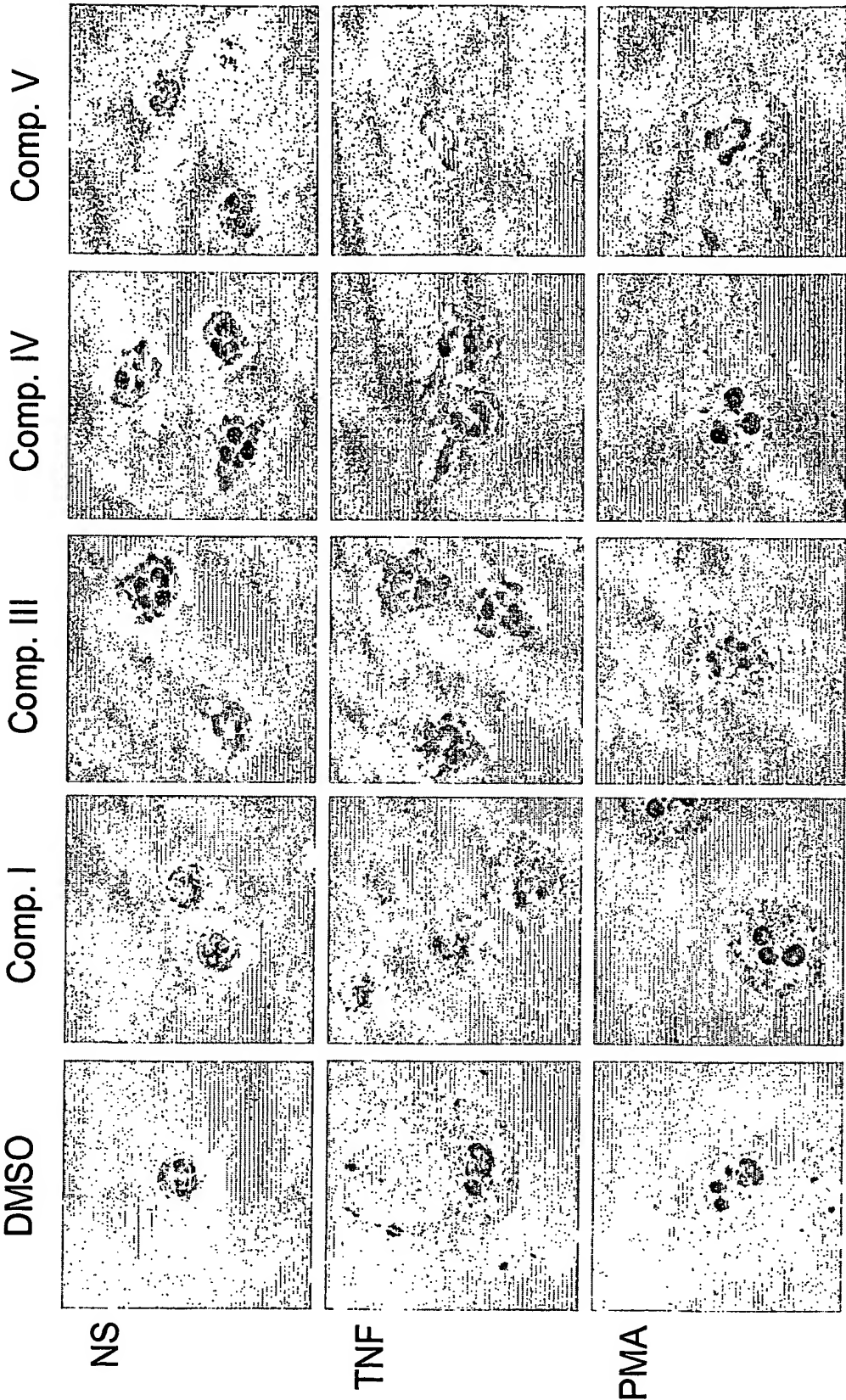


Figure 12B

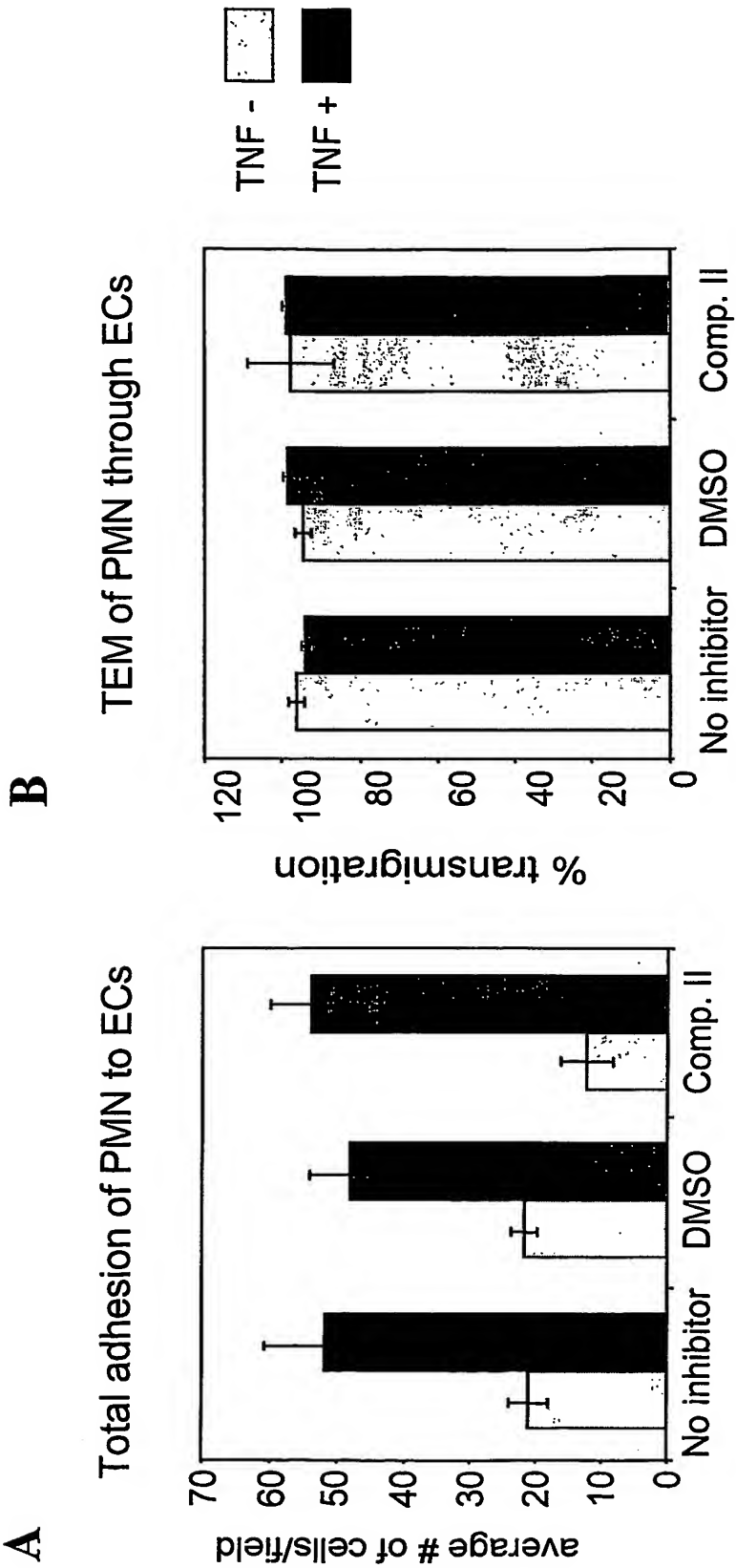


Figure 13



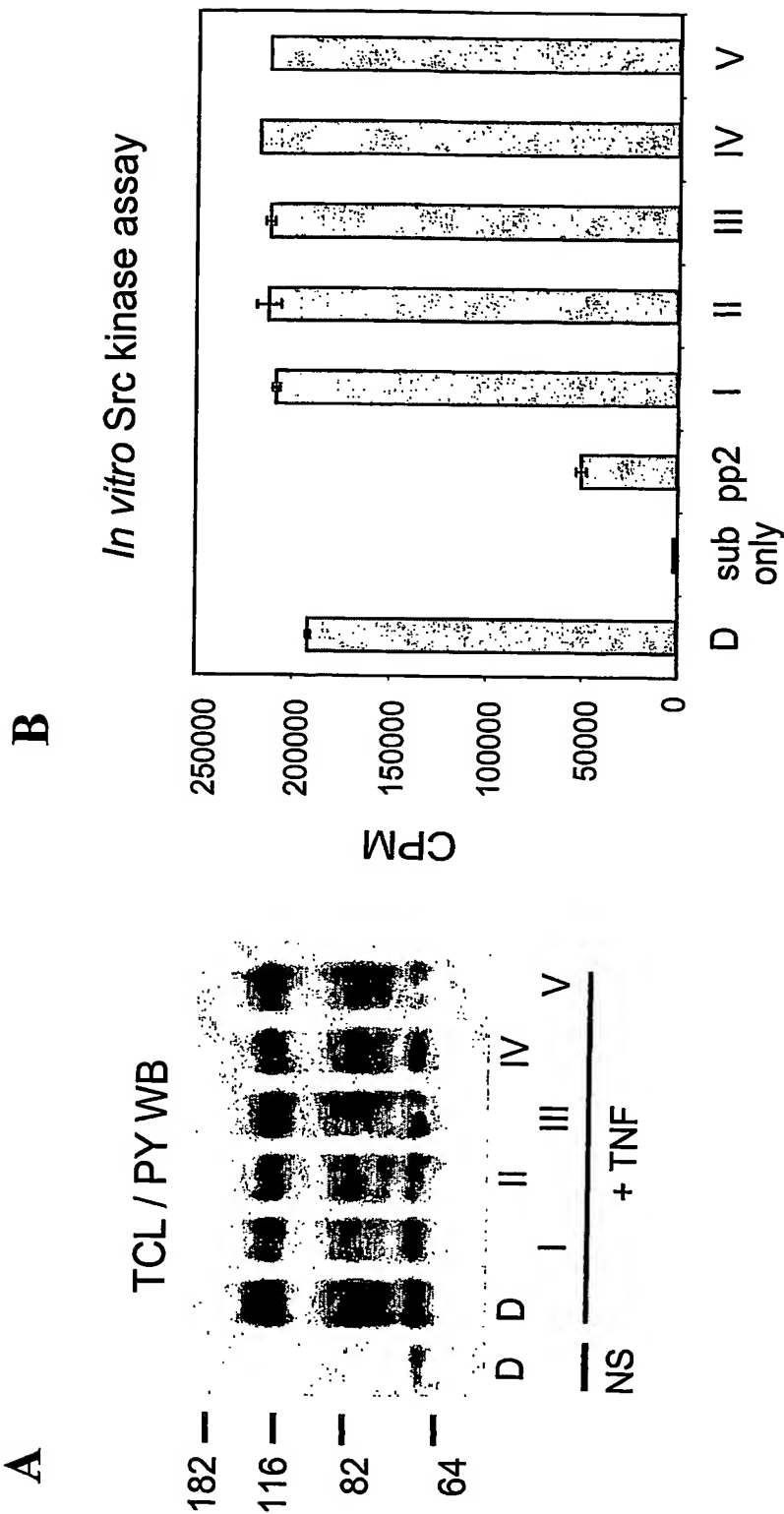


Figure 14A-B

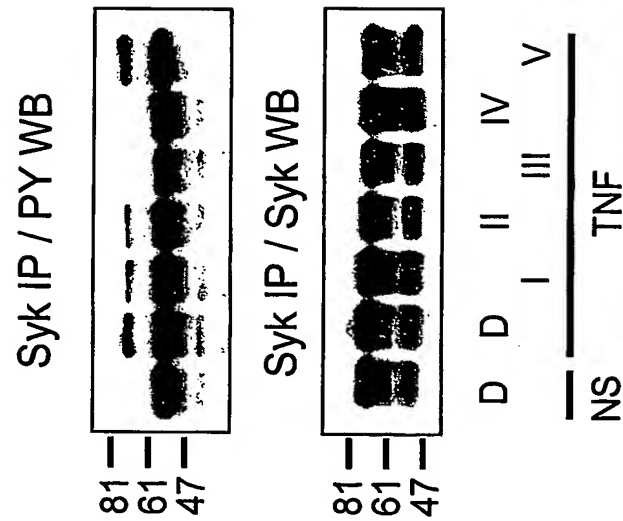
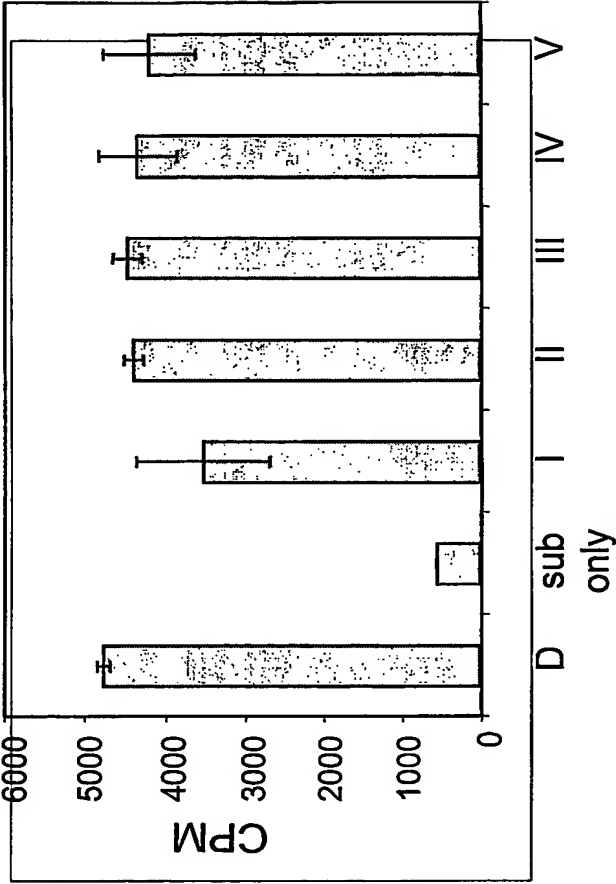


Figure 14C

*In vitro* Syk Kinase Assay



**Figure 14D**

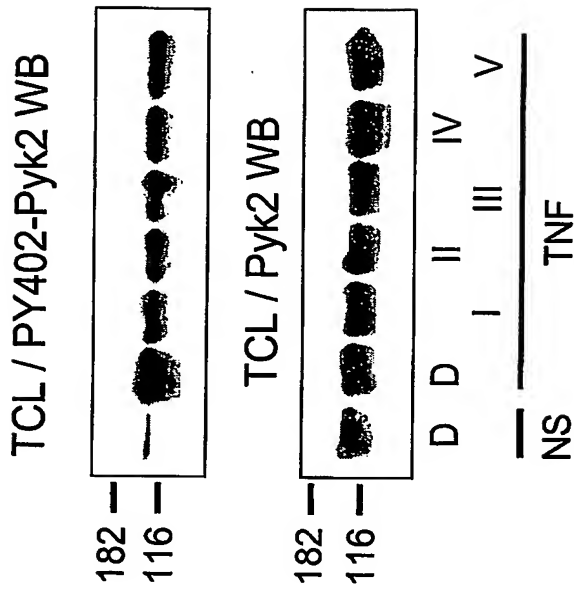


Figure 15

# Phagocyte oxidase (phox) (NADPH oxidase)

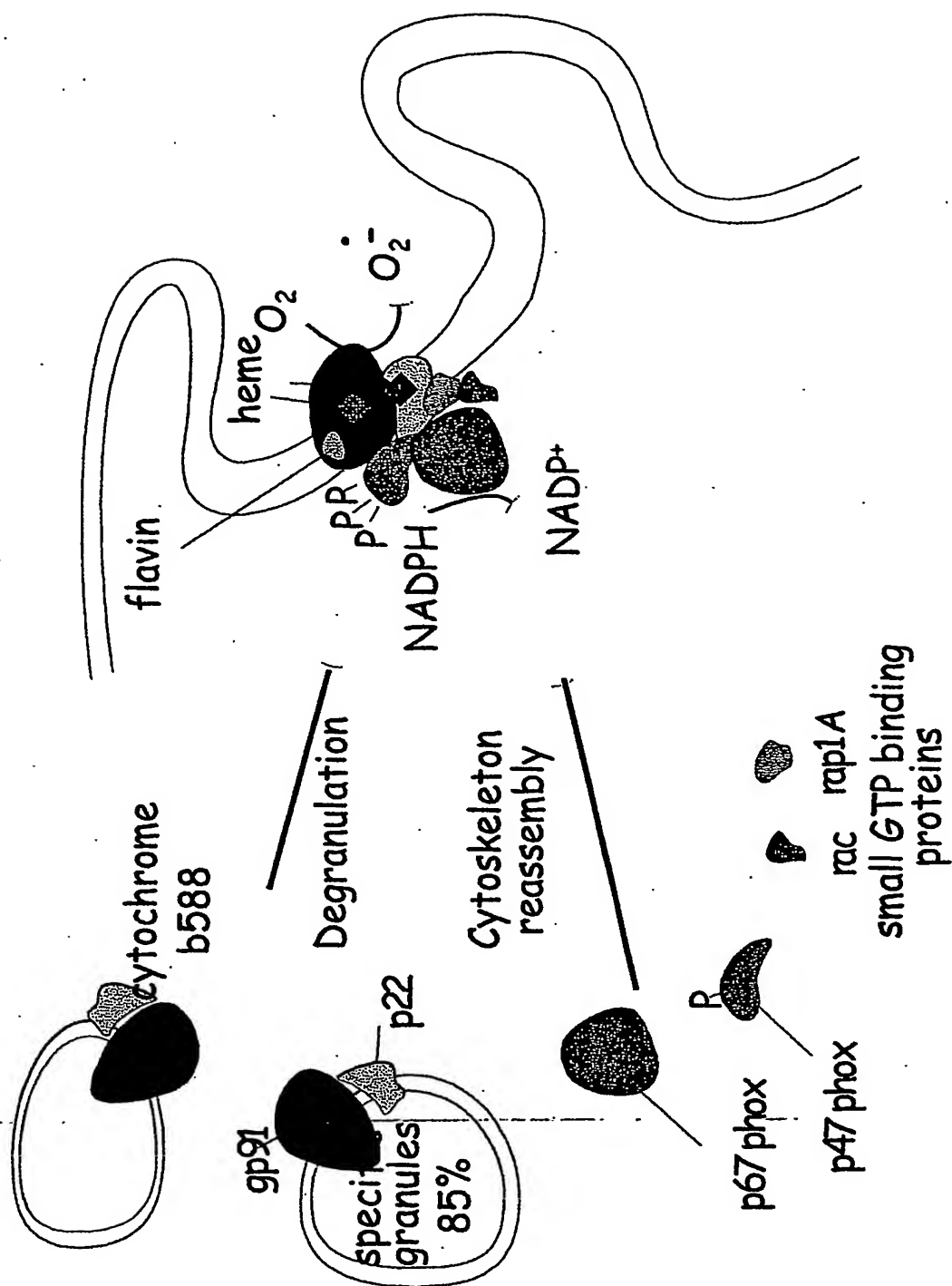
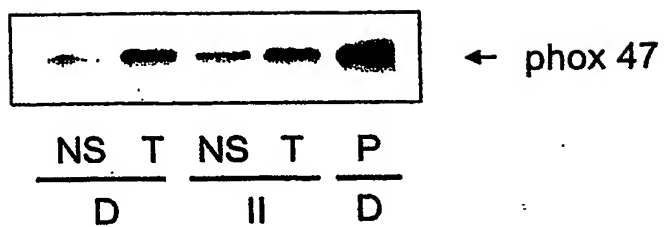


Figure 16

**Figure 17**

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